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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/955,801	09/19/2001	Rajneesh Taneja	ABB01259P00210US (6842.US)	1051
7590 02/14/2007 TAP Pharmaceutical Products, Inc. Attention: Mark J. Buonaiuto 675 North Field Drive Lake Forest, IL 60045			EXAMINER SHEIKH, HUMERA N	
			ART UNIT	PAPER NUMBER
			1615	
SHORTENED STATUTORY PERIOD OF RESPONSE		MAIL DATE	DELIVERY MODE	
3 MONTHS		02/14/2007	PAPER	

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary

Application No.

09/955,801

Applicant(s)

TANEJA ET AL.

Examiner

Humera N. Sheikh

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 06 December 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,3-17 and 19-21 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,3-17 and 19-21 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Status of the Application

Receipt of the Request for Continued Examination (RCE) and Applicant's Arguments/Remarks, all filed 12/06/06 and the Notice of Appeal filed 11/06/06 is acknowledged.

Applicant has overcome the following rejection(s) by virtue of the amendment and/or persuasive remarks filed 12/06/06:

The 35 U.S.C. §102(b) rejection of claims 1, 5, 6 and 17 over Kouchiwa *et al.* (EP 0 264 259) has been withdrawn.

The 35 U.S.C. §103(a) rejection of Claims 1-21 over Phillips (US Pat. No. 5,840,737) in view of GB 747,293 and further in view of Chen *et al.* (U.S. Pat. No. 6,544,556 B1) has been withdrawn.

Claims 1, 3-17 and 19-21 are pending in this action. Claims 1, 3 and 19 have been amended. Claims 2 and 18 have been cancelled. Claims 1, 3-17 and 19-21 are rejected.

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 12/06/06 has been entered.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1, 3-17 and 19-21 are rejected under 35 U.S.C. 102(e) as being anticipated by Phillips (U.S. Pat. No. 6,489,346 B1) (hereafter Phillips II).

The instant invention is drawn to a solid pharmaceutical formulation comprising: (a) a therapeutically effective amount of at least one acid labile pharmaceutical compound; and (b) a pharmaceutically acceptable protectant comprising (i) a water-soluble acid neutralizer; and (ii) a water-insoluble acid neutralizer.

Phillips II ('346) teaches a non-enteric coated solid pharmaceutical composition comprising a non-enteric coated proton pump inhibitor in a pharmaceutically acceptable carrier and at least one buffering agent and a method for treating acid-related gastrointestinal disorders comprising administering to a patient the non-enteric coated solid pharmaceutical composition. The pharmaceutically acceptable carrier comprises a bicarbonate salt of a Group IA metal and a carbonate salt of a Group IA metal (see Abstract; Claims); (col. 11, lines 36-44); (col. 13, line 47 – col. 14, line 26).

Phillips II teaches that mixtures of the buffering agents can be utilized (column 13, lines 47-53). Suitable buffering agents disclosed include sodium bicarbonate, potassium bicarbonate,

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magnesium hydroxide, aluminum hydroxide, aluminum hydroxide/sodium bicarbonate coprecipitate, sodium carbonate and calcium carbonate (see col. 13, line 63 – col. 14, line 14); (col. 17, lines 58-60).

The non-enteric proton pump inhibitors include a substituted benzimidazole of lansoprazole or an enantiomer, isomer, derivative, free base or salts thereof (see Abstract).

The instant invention is anticipated by Phillips.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1, 3-17 and 19-21 are rejected under 35 U.S.C. 103(a) as being unpatentable over by Kouchiwa *et al.* (EP 0 264 259) in view of Chen *et al.* (U.S. Pat. No. 6,544,556 B1).

The instant invention is drawn to a solid pharmaceutical formulation comprising: (a) a therapeutically effective amount of at least one acid labile pharmaceutical compound; and (b) a pharmaceutically acceptable protectant comprising (i) a water-soluble acid neutralizer; and (ii) a water-insoluble acid neutralizer.

Kouchiwa *et al.* ('259) teach stabilized, therapeutic pharmaceutical compositions comprising an active ingredient (dihydropyridines) in combination with one or more of *sodium carbonate*, sodium hydrogen carbonate, *calcium carbonate* and calcium hydrogen phosphate (see reference page 2, lines 1-32 and Abstract).

The stabilized compositions of the invention can be prepared by any suitable conventional means. Thus, for example, there may be added to the compound of formula (I) one or more of sodium carbonate, sodium hydrogen carbonate, calcium carbonate and calcium hydrogen phosphate, followed by addition of pharmaceutical auxiliary agents such as excipients, lubricants and disintegrants (page 2, lines 38-41).

A variety of pharmaceutical preparations, such as powders, tablets, capsules and granules can be formed from the resultant mixtures (page 2, lines 41-43).

Kouchiwa *et al.* teach a dihydropyridine derivative as the active ingredient for use in their invention. Kouchiwa *et al.* do not teach an acid-labile compound.

Chen *et al.* ('556) teaches pharmaceutical formulations comprising a non-steroidal anti-inflammatory drug (NSAID) and a proton pump inhibitor in an amount effective to inhibit gastrointestinal side effects (see Abstract).

Suitable NSAIDS disclosed include naproxen (a dihydropyridine-NSAID derivative). Suitable proton pump inhibitors disclosed include lansoprazole, omeprazole, pantoprazole and the like, including isomers, enantiomers and alkaline salts thereof (col. 6, lines 32-40).

Chen *et al.* teach that pH-buffering substances and alkaline compounds may be mixed with proton pump inhibitors and include aluminum hydroxide/sodium bicarbonate precipitate and substances normally used in antacid preparations such as aluminum, calcium and magnesium hydroxides (col. 9, lines 15-40).

The pharmaceutical compositions are preferably administered orally in oral dosage forms such as in the form of tablets, capsules, troches, lozenges, aqueous or oily suspensions, dispersible powders or granules, emulsions, multiparticulate formulations, syrups, elixirs and the like (column 4, lines 30-36); (col. 7, lines 22-30) and claims.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to incorporate suitable active ingredients, particularly acid-labile compounds such as taught by Chen *et al.* within the pharmaceutical compositions of Kouchiwa *et al.* One of ordinary skill in the art would be motivated to do so with a reasonable expectation of success because Chen *et al.* teach pharmaceutical formulations comprising NSAIDs in combination with acid labile compounds such as proton pump inhibitors and teach that their formulations are effective for treating an array of gastric acid-related diseases. The expected result would be a highly effective pharmaceutical formulation for treating gastric acid diseases.

Claims 1, 3-17 and 19-21 are rejected under 35 U.S.C. 103(a) as being unpatentable over GB 747,293 in view of Chen *et al.* (U.S. Pat. No. 6,544,556 B1).

The instant invention is drawn to a solid pharmaceutical formulation comprising: (a) a therapeutically effective amount of at least one acid labile pharmaceutical compound; and (b) a pharmaceutically acceptable protectant comprising (i) a water-soluble acid neutralizer; and (ii) a water-insoluble acid neutralizer.

GB '293 patent teaches a pharmaceutical composition comprising a therapeutically effective amount of an acid-labile compound (erythromycin) in combination with acid neutralizers and buffers (see reference column 1, line 14 – col. 3, line 6).

Suitable, physiologically acceptable acid neutralizers disclosed are *aluminum hydroxide*, calcium hydroxide, sodium acetate, magnesium trisilicate, sodium phosphate, *calcium carbonate*, *sodium bicarbonate* and *sodium carbonate* (col. 2, lines 78-85). The acid neutralizers (buffers) may be used alone or in suitable combinations (col. 3, lines 4-6). The composition provides for adequate blood levels, whereby pH levels are effectively maintained.

The GB '293 patent teaches liquid suspensions. The '293 reference does not teach "solid" formulations.

Chen *et al.* ('556) teaches pharmaceutical formulations comprising a non-steroidal anti-inflammatory drug (NSAID) and a proton pump inhibitor in an amount effective to inhibit gastrointestinal side effects (see Abstract). The pharmaceutical compositions are preferably administered orally in oral dosage forms such as in the form of tablets, capsules, troches,

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lozenges, aqueous or oily suspensions, dispersible powders or granules, emulsions, multiparticulate formulations, syrups, elixirs and the like (see column 4, lines 30-36); (col. 7, lines 22-30) and claims.

Chen *et al.* teach that pH-buffering substances and alkaline compounds may be mixed with proton pump inhibitors and include aluminum hydroxide/sodium bicarbonate precipitate and substances normally used in antacid preparations such as aluminum, calcium and magnesium hydroxides (col. 9, lines 15-40).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to incorporate oral, 'solid' dosage forms, such as taught by Chen *et al.* within the liquid formulations of the GB '293 patent. One of ordinary skill in the art would be motivated to do so with a reasonable expectation of success because Chen *et al.* teach that their oral dosage forms, which comprise proton pump inhibitors can be administered in effective and preferable dosage forms that include solid oral forms, such as tablets, granules or the like or alternatively in liquid oral forms such as suspensions or syrups to provide for the treatment of gastrointestinal side effects in a patient. The expected result would be improved and enhanced solid dosage form for the effective treatment of gastrointestinal disorders and conditions.

Claims 1, 3-17 and 19-21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Phillips (U.S. Pat. No. 5,840,737) (hereafter 'Phillips I') in view of Phillips (U.S. Pat. No. 6,489,346 B1) (hereafter Phillips II).

The instant invention is drawn to a solid pharmaceutical formulation comprising: (a) a therapeutically effective amount of at least one acid labile pharmaceutical compound; and (b) a

pharmaceutically acceptable protectant comprising (i) a water-soluble acid neutralizer; and (ii) a water-insoluble acid neutralizer.

Phillips I ('737) teaches a pharmaceutical composition and methods for treating and/or preventing gastrointestinal conditions comprising active ingredients of acid-labile compounds (*i.e.*, omeprazole, lansoprazole and derivatives thereof) and a bicarbonate salt of a Group IA metal, preferably sodium bicarbonate (see reference column 7, line 3 – col. 8, line 46); Abstract & Claims.

The composition is used for the treatment of gastrointestinal conditions, including duodenal ulcers, gastric ulcers, gastroesophageal reflux disease (GERD), erosive esophagitis, and the like (col. 8, lines 47-61).

According to Phillips, the sodium bicarbonate acts as an antacid and protects the acid-labile compound (*i.e.*, omeprazole) from acid degradation (col. 8, lines 34-37).

Phillips I teaches a water-soluble acid neutralizer (*i.e.*, sodium (bi)carbonate). Phillips does not teach a water-insoluble acid neutralizer, such as calcium carbonate or aluminum hydroxide and does not teach 'solid' pharmaceutical formulations.

Phillips II ('346) teaches a non-enteric coated solid pharmaceutical composition comprising a non-enteric coated proton pump inhibitor in a pharmaceutically acceptable carrier and at least one buffering agent and a method for treating acid-related gastrointestinal disorders comprising administering to a patient the non-enteric coated solid pharmaceutical composition. The pharmaceutically acceptable carrier comprises a bicarbonate salt of a Group IA metal and a

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carbonate salt of a Group IA metal (see Abstract; Claims); (col. 11, lines 36-44); (col. 13, line 47 – col. 14, line 26).

Phillips teaches that mixtures of the buffering agents can be utilized (column 13, lines 47-53). Suitable buffering agents disclosed include sodium bicarbonate, potassium bicarbonate, magnesium hydroxide, aluminum hydroxide, aluminum hydroxide/sodium bicarbonate co-precipitate, sodium carbonate and calcium carbonate (see col. 13, line 63 – col. 14, line 14); (col. 17, lines 58-60).

The non-enteric proton pump inhibitors include a substituted benzimidazole of lansoprazole or an enantiomer, isomer, derivative, free base or salts thereof (see Abstract).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to incorporate the solid pharmaceutical formulations of Phillips II ('346) which utilize both water soluble- and water-insoluble neutralizers within the pharmaceutical formulations of Phillips I ('737). One of ordinary skill in the art would be motivated to do so with a reasonable expectation of success because Phillips II explicitly teaches a solid proton pump inhibitor formulation comprising water soluble- (*i.e.*, sodium bicarbonate) and water-insoluble (*i.e.*, calcium carbonate) neutralizers and teaches that the neutralizers or buffering agents function to substantially prevent or inhibit acid degradation of the proton pump inhibitor by elevating pH of the stomach sufficiently to achieve adequate bioavailability of the drug to effect therapeutic action. The expected result would be a non-enteric coated formulation wherein the bioavailability of the proton pump inhibitor is preserved to provide for the effective treatment and/or prevention of gastric acid related disorders.

Pertinent Art:

The prior art made of record and not relied upon is considered pertinent to Applicant's disclosure:

US Patent No. 4,786,505 (Lovgren *et al.*) 11-1988

Response to Arguments

Applicant's arguments filed 12/06/06 have been fully considered and were found to be partially persuasive.

35 U.S.C. §102(b) rejection of claims 1, 5, 6 and 17 over Kouchiwa et al. (EP 0 264 259):

Applicant argued, "Claim 1 has been amended to recite that the pharmaceutical compound is acid labile. Kouchiwa et al. do not disclose at least one acid labile pharmaceutical compound."

Applicant's arguments have been fully considered, and were found to be persuasive, by virtue of the amendment incorporating the term 'acid labile'. Accordingly, the 35 U.S.C. §102(b) rejection of claims 1, 5, 6 and 17 has been withdrawn.

However, the claims have now been rejected over Kouchiwa et al. in view of Chen et al. (6,544,556). While Kouchiwa et al. do not teach an acid labile compound Chen et al. are relied upon for their teaching of pharmaceutical formulations comprising NSAIDs in combination with proton pump inhibitors. The formulations are effective for the treatment of gastrointestinal disorders.

35 U.S.C. §103(a) rejection of claims 1-21 over GB '293 in view of Chen et al. (USPN 6,544,556) :

Applicant argued, "The inventive concept of the present invention is that a solid pharmaceutical composition comprising a pharmaceutically acceptable protectant comprising a combination of a water-soluble acid neutralizer and a water-insoluble acid neutralizer exhibits superior protective qualities when administered to a patient in need of treatment thereof. The reason for this is that the combination of a water-soluble acid neutralizer and a water-insoluble acid neutralizer has been found to (a) increase pH levels in an acidic environment (such as the stomach) to a greater extent when compared to the use of either of these acid neutralizers alone; and (b) maintain the elevated pH levels for a greater time period in said acidic environment when compared to the use of either of these acid neutralizers alone (See, specification, page 5, lines 8-11). Increasing the pH levels in an acidic environment: (a) is comforting to the patient receiving said treatment; and (b) protects an acid-labile pharmaceutical compound from substantial degradation as it passes through the stomach (an acidic environment) to the upper intestinal tract.

The '293 patent discloses an oral suspension composition containing erythromycin, a buffer and a suspending agent. The buffer may be any acid neutralizing base or salt of a strong base or salt of a strong base and a weak acid. While the specification of the '293 patent states that "we may use any of the buffers alone or we may use a suitable combination of buffers," nowhere does the '293 patent disclose, suggest or teach the importance of a combination of a water-soluble acid neutralizer and a water-insoluble acid neutralizer. Even if a skilled artisan practicing the '293 patent selected a water-soluble acid neutralizer and a water-insoluble acid neutralizer, such a selection would be completely serendipitous. The art does not disclose or suggest or teach the importance of a combination of a water-soluble acid neutralizer and a water-insoluble acid neutralizer. Chen et al. is silent about the importance of the combination of a water-soluble acid neutralizer and a water-insoluble acid neutralizer. Not only does Chen et al. not disclose the combination of a water-soluble acid neutralizer and a water-insoluble acid neutralizer, it employs an altogether different method to protect a proton pump inhibitor, namely, an enteric coating.

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The specification of the present invention states that it is preferable that the claimed formulations or pharmaceutical compounds included in the formulations not be enterically coated.”

Applicant’s arguments have been fully considered but were not found to be persuasive. Applicant essentially argues that the prior art does not suggest or teach the importance of combining both water-soluble as well as water-insoluble acid neutralizers. This argument was unpersuasive since the art explicitly teaches that combinations of the water-soluble and water-insoluble components can be utilized in their invention (see for instance, col. 3, lines 4-6 of ‘293). Thus, since the art teaches that combinations of the water soluble and water-insoluble neutralizers can be used, the art vividly recognizes the advantages and beneficial effects obtained from combining water soluble- and insoluble neutralizers. The teaching of a combination of water soluble- and insoluble neutralizers is sufficient to meet the instant claim requirements.

With regards to the instant invention’s “superior protective qualities” due to, for example, increase in pH levels argued by Applicant, it is noted that the claims are silent in reference to any mention of pH. The claims are generic in this matter.

Regarding Applicant’s argument that “Chen teaches enterically-coated proton pump inhibitor”, whereas the instant specification prefers *non*-enterically coated, the Examiner notes that the instant claims do not exclude the presence of an enteric coating. Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

35 U.S.C. §103(a) rejection of claims 1-21 over Phillips (USPN 5,840,737) in view of

GB 747,293:

Applicant's arguments have been considered and were found to be persuasive.

Accordingly, the 35 U.S.C. §103(a) rejection of claims 1-21 over Phillips (USPN 5,840,737) in view of GB 747,293 has been withdrawn.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Humera N. Sheikh whose telephone number is (571) 272-0604. The examiner can normally be reached on Monday through Friday during regular business hours.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward, can be reached on (571) 272-8373. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have any questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).


HUMERA N. SHEIKH
PRIMARY EXAMINER

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February 01, 2007